CHARGE NUMBER: 2500

PROGRAM TITLE: Synthesis of Tobacco Additives

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PROJECT LEADER: E. B. Sanders

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I. FLAVOR-RELEASE CHEMISTRY

A procedure was established for the isolation of pure guiacyl β-D-glucopyranoside utilizing ion exchange chromatography. Vanillin 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (CR-1436) and p-cresyl β-D-glucopyranoside (CR-1493) were added to the CR-file.[1]

A 50 g sample of poly(isopropenyl acetate) has been prepared and submitted to Development for evaluation as a potential acetic acid-release agent. Approximately 150 g of poly(allyl 3-methyl-1-butene-3-yl carbonate) has been prepared *via* polymerization of the corresponding monomer. The sample has been turned over to Gus Keritsis for incorporation into a suitable sheet material for evaluation as an isoprene-release system.[2]

The phenyllithium mediated condensation of tetramethylpyrazine with benzaldehyde has given a good yield of 1-phenyl-2-(3,4,6-trimethyl-2-pyrazinyl)ethanol.[3] Pyrolysis of the product at 480° gave benzaldehyde in about 80% yield and tetramethylpyrazine in about 70% yield.[1] This compound represents the first successful synthesis of a pyrazine-release system.

II. ALKALOID CHEMISTRY

A number of reducing agents have been tried in order to maximize the amount of *cis*-3'-methylnicotine from the reduction of 3'-methylmyosmine. The best result (6:4 *cis/trans*) was obtained *via* catalytic reduction over Raney nickel in ethanol containing sodium hydroxide. The compound will be purified by elution chromatography subsequent to methylation. A sample of *trans*-3'-methylnicotine was prepared by tosylation of *trans*-3'-hydroxymethylnicotine followed by reduction of the tosylate. The following compounds were added to the CR-file: 2-(4-nitrophenyl)-1,2-pyrroline (CR-1484), 1-methyl-2-(4-methylphenyl)pyrrolidine

(CR-1485), 2-(2-methylphenyl)-1,2-pyrroline (CR-1487), N'-methyl-2-methylanatabine (CR-1488), 2-(3-nitrophenyl)-1,2-pyrroline (CR-1489), 2-(2-methylphenyl)-pyrrolidine (CR-1490), 1-(1-pyrrolidinyl)-2-(2-pyridyl)propane (CR-1491), and 1-(2-ethyl-3-picolyl)pyrrolidine (CR-1492).[4]

A sample of 4-carbethoxypyrrolizidin-2,3-dione was prepared by condensation of ethyl (2-pyrrolidinyl)acetate with diethyl oxalate. Attempts were made to remove the carbomethoxy group by hydrolysis and decarboxylation using a wide assortment of reagents. Low yields, at best, of the desired dione were obtained.[5]

III. AMINO SUGAR CHEMISTRY

The thermolysis of aqueous solutions of 2-deoxy-2-amino-D-glucose was carried out for 15, 60 and 240 min at 100 and 150°. Each sample following thermolysis was separated into insoluble, soluble dialyzable, and soluble nondialyzable fractions. All three fractions contained approximately the same percentage of C, H, N, and O according to elemental analyses. Thermolysis at 150° for 60 min gives about equal amounts of all three fractions. Consequently these conditions will be used for large scale work.[6]

Studies have been initiated to convert 2-deoxy-2,5-fructosazine into 2,5-dideoxy-2,5-fructosazine. Two procedures which are being investigated are the direct reductive cleavage of the hydroxyl group using hydroiodic acid and reduction of the pyrazine ring to the dihydropyrazine system using sodium hydrosulfite followed by acid catalyzed dehydration to give the desired product. Both reactions are presently under investigation.[6]

Reaction of 1,2-dideoxy-1,2-diamino-D-glucitol with benzil has been carried out to give 2,3-diphenyl-5-tetrahydroxybutyl-5,6-dihydropyrazine. The structure of the product has been confirmed by nmr and mass spectra. Treatment of the dihydropyrazine with acetic acid led to rapid disappearance of the starting material to give two products which have not yet been characterized.[3]

IV. CUSTOM SYNTHESIS

Large-scale synthesis of guiacyl β-D-glucopyranoside has been initiated . Synthesis of the tetraacetyl glycoside has been completed, and the desired product will shortly be obtained using ion exchange chromatography.[7]

V. MISCELLANEOUS

The glue stripper program is essentially complete experimentally. Four optimized stripping systems have been developed. All four have been compared with one another and with Magnus 642-D, the best commercial formulation. All four systems outperformed the Magnus 642-D.[8]

VI. REFERENCES

1.	Armstrong, D. D.	7021
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3.	Houminer, Y.	7098
4.	Secor, H. V.	7126
5.	Edwards, W. B.	7113
6.	Kite, G. F.	7124
7.	DeBardeleben, J. F.	7101
8.	Van Auken, T. V.	7100

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